SECTION 2 NON-TECHNICAL ABSTRACT

Prostate cancer is the most commonly diagnosed malignancy in men. Although conventional therapies (surgery and radiation therapy) produce high cure rates of early stage prostate cancer, many tumors recur and metastasize. There is a real need to develop new therapies that may improve the effectiveness of conventional cancer therapies.

In light of this, we have developed a novel, multi-faceted gene therapy approach for the treatment of prostate cancer. Our approach utilizes a modified cold virus, called an adenovirus, to deliver a pair of therapeutic genes to prostate tumors. The virus itself generates a potent anti-tumor effect by preferentially replicating in and destroying prostate tumor cells. The tumor-specific killing effect of the virus can be enhanced by combining it with a form of tumor-targeted chemotherapy called suicide gene therapy. Activation of the suicide genes renders malignant cells sensitive to specific chemical agents (prodrugs) and sensitizes them to the therapeutic effects of radiation. A Phase I clinical trial that evaluated the safety of combining viral therapy with suicide gene therapy in men with recurrent prostate cancer has been completed. Overall, the treatment was well tolerated. Most of the side-effects observed were expected, considered minimal to mild, and lasted less than one week.

The study described here is a follow up of the previous Phase I trial. In this study, the safety of combining viral and suicide gene therapies with standard radiation therapy will be evaluated in men with locally advanced prostate cancer. Such patients have a high likelihood that radiation therapy alone will not eliminate the cancer. The virus will be injected into the prostate gland under ultrasound guidance. Two days later, patients will be administered two prodrugs for one to four weeks and will receive standard external beam radiation therapy. The primary objective of this study is to determine whether the combined treatment is safe for use in humans.